REMARKS

The present invention relates to novel Rh(D) binding proteins, preferably, antibodies, and DNA encoding such proteins. The invention further relates to vectors and cells comprising the DNA and proteins of the invention as these are useful for, *inter alia*, novel diagnostic assays and the development of therapeutics. The invention also includes methods of generating the novel proteins and DNAs of the invention.

This application is a divisional of U.S. Patent Application No. 09/240,274 (the "parent" application), now issued as U.S. 6,255,455. More specifically, the present application relates to novel nucleic acids encoding the novel proteins of the invention, where claims reciting the novel proteins have now issued in the '455 patent. More specifically, by way of preliminary amendment, claims 1-10 and 15-21 were canceled such that claims 11-14, which were the claims of Group III as restricted by way of Restriction Requirement mailed March 16, 2000, in the parent application, were selected for prosecution in this application. Further, claims 22-37, which recite subject matter related to claims 11-14, were added in the Preliminary Amendment.

Claims 14, 22-24, 27-32 and 35-37, drawn to a non-elected invention following election per the Restriction Requirement mailed June 20, 2003 (Paper No. 4) in this application, have been canceled herein, as has claim 13. Further, new claims 38-51, drawn to the elected invention, have been added herein. As more fully set forth below, new claims 38-51 are fully supported by the specification as filed and add no new matter.

Claims 11, 12, 25, 26, and 33-34 have been amended, among other things, in accordance with the species election required in Paper No. 4 in that the nucleotide sequence of the nucleic acid encoding a novel protein of the invention is SEQ ID NO:97, which, as correctly pointed out by the Examiner at page 2 of the Office Action, encodes a protein of amino acid sequence SEQ ID NO:28, designated as heavy chain "E03" in the application. As more fully discussed below, no new matter has been added by way of these amendments.

In sum, after entry of the instant Amendment, amended claims 11, 12, 25, 26, 33, 34, and new claims 38-51, are under examination in this application.

Rejection of claims 11-13, 25-26 and 33-34 under 35 U.S.C. § 112, second paragraph

Claims 11-13, 25-26 and 33-34 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner is of the opinion that claims 11-13,

25-26 and 33-34 are indefinite for the use of a successive series of open-ended language, i.e., claim 11 recites a DNA "having (a sequence) comprising."

Applicant, while not necessarily agreeing with the Examiner's reasoning, but rather in a good faith effort to expedite prosecution of this application, has amended claims 11, 12, 25-26 and 33-34, to remove the terms "having" and "comprising", thereby rendering this rejection moot as to these claims. Claim 13 having been canceled, the rejection is also mooted as to this claim. Thus, the rejection under 35 U.S.C. § 112, second paragraph, should be reconsidered and withdrawn as to claims 11, 12, 25-26, and 33-34.

Rejection of claims 11-13, 25-26 and 33-34, under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 11-13, 25-26 and 33-34, under 35 U.S.C. §112, first paragraph, as lacking written description. The Examiner is of the opinion that the specification does not sufficiently describe the functional gene per se (i.e., 5' and 3' flanking sequences) or any other sequences than those sequences disclosed in the as-filed specification. Thus, the Examiner reasons that Applicant is not entitled to claim more than the disclosed sequences. Applicant respectfully traverses this rejection for the following reasons.

Preliminarily, claim 13 has been canceled herein, and any rejection of this claim has thus been rendered moot. Further, Applicant, while not necessarily agreeing with the Examiner's reasoning, but in a good faith effort to expedite prosecution of this application, has amended the claims to recite that the novel DNA encodes a human anti-Rh(D) antibody, and the claims further recite that the nucleotide and amino acid sequences of the DNA are selected from groups of sequences all of which were disclosed in the specification as filed and which are identified using a SEQ ID NO sequence identifier. These amendments are fully supported by the specification as filed, wherein all of the sequences recited in the claims were disclosed and set forth throughout the specification, including, but not limited to, at page 66, line 1, to page 126, line 23, and Figures 10 and 11. Accordingly, no new matter has been added by way of these amendments. Applicants respectfully submit that claims 11, 12, 25, 26, 33-34, as amended, and new claims 38-51 are enabled under 35 U.S.C. 35 U.S.C. §112, first paragraph, notwithstanding the case law cited by the Examiner in support of this rejection as more fully discussed as follows.

The Examiner has cited *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991), as supporting this rejection that there was insufficient written description in this

application. In *Vas-Cath*, the Court of Appeals for the Federal Circuit traced the development of the written description requirement under 35 U.S.C. §112, first paragraph. The *Vas-Cath* Court, in a unanimous opinion, noted approvingly that in a written description analysis, "[t]he primary concern is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure." *Vas-Cath*, 19 USPQ2d at 1116 (quoting *In re Wertheim*, 191 USPQ 90, 96 (C.C.P.A. 1976)). After discussing the policy reasons underlying the requirement, the Court set forth the standard for the written description requirement:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. . . . The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter."

Vas-Cath, 19 USPQ2d at 1117 (emphasis added) (quoting *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 227 USPQ 177, 179 (Fed. Cir. 1985)). *Accord University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). Therefore, it is well-settled that the knowledge of those skilled in the art informs the written description inquiry.

Applicant respectfully submits that the claims, as amended, reciting an isolated DNA encoding a human anti-Rh(D) antibody where the nucleotide sequence of the DNA is selected from the group consisting of SEQ ID Nos:70-138 and 182-224 (heavy chains) and an isolated DNA encoding a human anti-Rh(D) antibody wherein the amino acid sequence of the antibody is selected from the group consisting of SEQ ID Nos: 1-69 and 139-181, are completely supported by the specification as filed and satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, under current law. Particularly, the claimed nucleic acids and peptides encoded thereby are described by both biological and chemical properties in that the representative species, *e.g.*, nucleic and amino acid sequences, are disclosed for one-hundred and twelve anti-Rh(D) antibodies of the invention. Further, the specification as filed disclosed, and the amended claims recite, that the novel nucleic acids encode a protein comprising a known biological activity, *e.g.*, capable of specifically binding Rh(D) antigen. Additionally, the specification discloses numerous assays for assessing the biological activity(ies) of the novel nucleic acids, and proteins encoded thereby, and many other such assays were also known to

those in the art at the time the specification was filed. These properties more than satisfy the written description requirement and provide ample support a recite a genus claim under 35 U.S.C. §112, first paragraph. At the very least, the disclosure provided by the specification as filed provides ample written description to support the claims as amended under the statute.

Additionally, Applicant has not found a single case which holds that the each and every species, *e.g.*, each nucleic acid sequence or each amino acid sequence of a peptide, must be disclosed in order to satisfy the written description requirement. Indeed, in *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976), the court held that Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art." (Emphasis added.) Further, the cases cited by the Examiner do not support this conclusion for the reasons set forth below.

In *Regents of the Univ. of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), cited by the Examiner in support of this rejection and which is a landmark case relating to written description in the context of amino and nucleic acids, the Court of Appeals for the Federal Circuit held that a description of the amino acid sequence of the A and B chains of human insulin did not provide a written description of human insulin cDNA where no part of the nucleic acid sequence of human insulin was disclosed. That is clearly not the case here where the entire nucleic and amino acid sequences of over one-hundred (112) anti-Rh(D) antibodies are disclosed, there has been extensive reduction to practice, and where the binding characteristics of the anti-Rh(D) antibodies have been identified.

Further, the adequacy of the disclosure provided in the specification must be considered in light of the advanced state of knowledge in the relevant art and because there has been extensive reduction to practice, *e.g.*, 112 nucleic and amino acid sequences have been disclosed in the specification as filed. That is, the skilled artisan, once provided with the disclosure of the specification as filed, including the numerous sequences provided, would have understood that Applicant was in possession of the claimed invention as recited in claims 11-12, 25, 26, 33-34, and 38-51. Thus, the holding of *Regents of the Univ. of California v. Eli Lilly & Co.*, is inapposite under the present facts where there is extensive sequence data to provide ample written description of the subject matter of the rejected claims.

Whatever the holding of *Regents of the Univ. of California v. Eli Lilly & Co.*, the case is not applicable under the facts under consideration herein, where the nucleic and amino acid sequences of one-hundred and twelve anti-Rh(D) antibodies are disclosed, and where the

specification as filed discloses numerous assays for determining if the antibody has the requisite biological activity(ies).

Similarly, *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993), a case cited by the Examiner in support of the rejection for lack of written description, is also not applicable under the present facts. *Fiers v. Revel* involved a three-way interference proceeding where inventor Revel was denied priority based on a foreign filing. The Federal Circuit Court of Appeals held that Revel's claim for priority was defective for failure to provide sufficient written description where he claimed DNA coding for beta-interferon (b-IF) based only on a partial amino acid sequence of the protein and a method for isolating mRNA coding for b-IF based on the partial protein sequence. Clearly, *Fiers v. Revel* is not applicable under the facts presented herein where the nucleic and amino acid sequences of one-hundred and twelve anti-Rh(D) antibodies have been disclosed, and where numerous assays for determining the binding characteristics of the antibodies have been set forth.

The Examiner has also cited *Amgen v. Chugai Pharm. Co.*, 18 USPQ2d 1016 (Fed. Cir. 1991), in support of the rejection of the claims for lack of written description. Preliminarily, Applicant respectfully points out that *Amgen* is a lack of enablement case, which is not applicable to a written description analysis. Nevertheless, Applicant respectfully submits that *Amgen v. Chugai* is not relevant under the facts of the present application since the *Amgen* Court analyzed the enablement requirement in the context of a claim for all nucleic acids encoding analogs of erythropoietin (EPO) based on disclosure of only a partial amino acid sequence of human EPO. That is, the claim at issue in *Amgen* was similar to that in *Eli Lilly* in that the claim recited DNA sequences where the specification only disclosed an amino acid sequence. Discussing the lack of enablement under 35 U.S.C. §112, first paragraph, the *Amgen* Court noted:

> In affirming the district court's invalidation of claims 7, 8, 23-27, and 29, under Section 112, we do not intend to imply that generic claims to genetic sequences cannot be valid where they are of a scope appropriate to the invention disclosed by an applicant. That is not the case here, where Amgen has claimed every possible analog of a gene containing about 4,000 nucleotides, with a disclosure only of how to make EPO and a very few analogs. *Amgen,* 18 USPQ2d at 1027 (emphasis added).

The holding of *Amgen* is inapplicable under the facts set forth herein. That is, disclosure in the instant specification discloses the nucleic and amino acid sequences of one-hundred and twelve anti-Rh(D) antibodies. Further, unlike EPO, Applicant has disclosed extensive sequence data regarding anti-Rh(D) antibodies, including the identification by Applicant of the binding characteristics of the anti-Rh(D) antibodies. Moreover, there are several assays used to determine the biological activity of the anti-Rh(D) antibodies encoded by a nucleic acid of interest, which are set forth in the specification and/or are well-known in the art.

Fiddes v. Baird, 30 USPQ2d 1481 (Bd. Pat. App. & Int. 1993), also cited by the Examiner in support of this rejection, is also easily distinguished from the present facts. In *Fiddes v. Baird*, the Board of Patent Appeals and Interferences, finding in favor of Fiddes in the interference proceeding, found that Baird's claims to a mammalian fibroblast growth factor (FGF) were unpatentable as lacking written description. The Board noted:

> In our view, the '455 patent does not contain a written description for the broad class of mammalian FGFs. The patent teaches no amino acid or DNA sequences for any mammalian FGF other than bovine pituitary FGF. For bovine pituitary FGF the patent teaches both the amino acid sequence and a theoretical DNA sequence for the factor. The patent does not teach the naturally occurring gene encoding the factor and thus, Baird was not in possession of the naturally occurring gene encoding bovine pituitary FGF. Nor was he in possession of either the amino acid sequence for any other mammalian FGF or any naturally occurring gene encoding any mammalian FGF other than bovine pituitary FGF. Thus Baird was not in possession of the genes encoding mammalian FGFs since in 1987, knowledge of the amino acid sequence of a protein coupled with the established relationship in the genetic code between a nucleic acid and the protein it encodes would not establish possession in the gene encoding that protein.

Fiddes v. Baird, 30 USPQ2d at 1483. The Board further noted that once the nucleic acid sequence of bovine pituitary FGF was determined, Baird's theoretical DNA sequence differed from the naturally occurring sequence at 51 out of 146 codons. *Id.* Thus, the Board found that where no nucleic acid sequence whatsoever was disclosed and where only one amino acid sequence was set forth, the application as filed would not support, in essence, claims reciting a DNA molecule encoding mammalian basic FGF.

The facts of *Fiddes v. Baird* are inapposite to the situation at hand. In the instant application, the specification discloses novel nucleic acids encoding one-hundred and twelve anti-Rh(D) antibodies, and the specification discloses extensive assays for determining biological activity of the antibodies. Thus, unlike the facts of *Fiddes v. Baird*, the instant application amply supports claims reciting an isolated DNA encoding a human anti-Rh(D) antibody, in light of the extensive disclosure provided in the specification as filed, and in further view of the high degree of knowledge in the relevant art, which informs the written description inquiry of Section 112, first paragraph.

Therefore, even assuming, *arguendo*, that *Amgen v. Chugai*, *Fiers v. Revel*, and/or *Fiddes v. Baird*, are somehow applicable in view of the extensive disclosure provided by the instant application, the disclosure in the instant application clearly apprises one skilled in the art that Applicant was in possession of the claimed invention at the time the specification was filed for purposes of 35 U.S.C. §112, first paragraph. This is because the skilled artisan, to whom the application is addressed, armed with the teachings provided by the specification as filed and the knowledge of the prior art, would have reasonably understood that the invention encompasses, at the very least, an isolated DNA encoding all one-hundred twelve anti-Rh(D) antibodies. As noted previously elsewhere herein, the written description requirement must be analyzed in context of the knowledge of the skilled artisan, which in this case includes extensive sequence data disclosed in the specification as filed regarding nucleic acids encoding anti-Rh(D) antibodies. This is especially true where the specification provides extensive reduction to practice, including, but not limited to, myriad working examples of the claimed nucleic acids and proteins encoded thereby, and numerous assays that can be used to identify additional nucleic acids encoding peptides of the invention. Given the advanced state of the relevant art and the extensive disclosure provided by the specification as filed, the claims of the present application are amply supported and satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Applicant respectfully submits that the extensive disclosure and reduction to practice demonstrated by the specification as filed provides ample written description for claims reciting an isolated DNA encoding a human anti-Rh(D) antibody. The specification describes, for the first time, numerous novel nucleotide sequences that encode an antibody and that can bind to Rh(D) and other Rh antigens. Further, Applicant does not understand the Examiner's

assertion that only "an isolated polynucleotide consisting of SEQ ID NO:97 and an isolated anti-Rh(D) protein of SEQ ID NO:28" has been provided by the disclosure of the specification as filed. Indeed, the nucleotide and amino acid sequences of one-hundred and twelve anti-Rh(D) proteins were set forth in the specification as filed and the written description requirement of 35 U.S.C. §112, first paragraph, has certainly be satisfied at the very least with regard to these proteins. The claims as amended, recite only the sequences disclosed in the specification as filed, and the written description requirement has been satisfied as to these claims, if not to claims reciting a genus based on such extensive disclosure of numerous species. Therefore, at the very least, the claims as amended are certainly supported for purposes of the written description requirement.

In sum, Applicant respectfully submits that the specification as filed amply supports claims reciting an isolated DNA encoding a anti-Rh(D) antibody. Further, Applicant respectfully submits that the skilled artisan would have understood, based upon the disclosure provided in the specification as filed, that the invention includes, at the very least, an isolated DNA encoding a human anti-Rh(D) antibody, wherein the amino acid sequence of said human anti-Rh(D) is selected from the group consisting of SEQ ID Nos: 1-69 and 139-181 (claim 11). Further, the skilled artisan would have also understood that the invention includes an isolated DNA encoding a human anti-Rh(D) where the nucleotide sequence of the DNA is selected from SEQ ID Nos: 70-138 and 182-224 (claim 12). The remaining claims under examination in the instant application depend from these two claims and are fully supported by the specification as filed. Therefore, there is ample support in the specification as filed for claims reciting, *inter alia*, an isolated DNA encoding a human anti-Rh(D) antibody, and these claims satisfy the written description requirement of 35 U.S.C. §112, first paragraph. Therefore, the rejection of claims 11, 12, 25, 26, and 33-34 (claim 13 having been canceled herein) under this statute should be reconsidered and withdrawn.

New claims 38-51

New claims 38-51 recite, *inter alia*, vectors and recombinant cells comprising the nucleic acids of the invention as recited in claims 11, 12, 25, 26, 33, and 34, as now amended to recite the amino and nucleic acid sequences explicitly disclosed in the specification as filed. Applicant respectfully asserts that ample support for vectors and cells comprising these

sequences, as well as cells comprising the vectors which, in turn, comprise the sequences, are found in the specification as filed. Indeed, the specification as filed is replete with numerous examples where the nucleic acids of the invention have been cloned into vectors and introduced into a wide plethora of cells. Further, commencing on page 11, at line 16, the specification details the various recombinant techniques, including the use of vectors and recombinant cells, in the methods of the invention, and the specification cites, among others, at page 12, lines 11-12, a well-known treatise relating to such methods, *i.e.*, Sambrook et al. (1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor, NY). Therefore the specification fully supports vectors and cells comprising sequences of the present invention as now recited in claims 38-51, and the addition of these claims adds no new matter.

Summary

Applicant respectfully submits that each rejection of the Examiner to the claims of the present application has been either overcome or is now inapplicable, and that each of claims 11, 12, 25, 26, 33, 34, and 38-51, is in condition for allowance. Reconsideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,

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February 18, 2004
Date

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Enclosure: (Petition for Two Month Extension of Time and fee therefor)